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REVIEW ARTICLE

THE ROLE OF ALLULOSE AND SUGAR ALCOHOLS IN GUT MICROBIOTA MODULATION AND METABOLIC HEALTH: A REVIEW

Mostafa Essam Eissa🗅

Independent Researcher and Consultant, Cairo, Egypt.

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Abstract



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*Address for Correspondence:

Dr. Mostafa Essam Eissa, Independent Researcher and Consultant, Cairo, Egypt. Tel: +20100615485; E-mail: mostafaessameissa@yahoo.com

INTRODUCTION

The global obesity epidemic has spurred a relentless search for healthier alternatives to traditional sugar. Consumers are increasingly seeking sweeteners that can satisfy their sweet tooth without the detrimental health consequences associated with excessive sugar intake. Allulose and sugar alcohols have emerged as promising candidates in this quest for low-calorie sweetness¹. While artificial sweeteners have offered a solution for decades, concerns over their potential long-term health effects have prompted a search for more natural and benign alternatives². Allulose and sugar alcohols have emerged as promising candidates, offering a sweet taste without the caloric burden and potential health risks associated with traditional sugar and artificial sweeteners³. These low-calorie sweeteners have gained significant attention for their potential to improve metabolic health, modulate gut microbiota, and provide a satisfying taste experience⁴⁻⁶. Table 1 provides a comparison between the ordinary sucrose alternatives.

The gut microbiota: A key player in health and disease

The human gut houses a diverse community of microorganisms, collectively known as the gut

Allulose and sugar alcohols, like erythritol and xylitol, are low-calorie sweeteners gaining attention for their potential to positively influence metabolic health. This brief review explores how these sweeteners can shape the gut microbiota. Acting as prebiotics, they can foster the growth of beneficial bacteria and stimulate the production of short-chain fatty acids. These effects may contribute to improved insulin sensitivity, reduced inflammation and a stronger gut barrier. However, excessive sugar alcohol intake can lead to digestive discomfort. Further research is needed to assess the long-term impact of these sweeteners on gut microbiota and metabolic health, as well as their interactions with other dietary factors. By understanding the intricate relationship between these sweeteners, gut microbiota and metabolic health, it will be possible to develop well-informed dietary guidelines to optimize health and well-being.

Keywords: Allulose, gut microbiota, maltitol, prebiotics, sorbitol, xylitol.

microbiota⁷. This intricate ecosystem significantly influences human health, impacting digestion, metabolism, and immune function. A balanced and varied gut microbiota is key to optimal well-being⁸. However, dietary choices, lifestyle factors, and antibiotic use can disrupt this delicate balance, leading to dysbiosis and potential health issues⁹. To promote a healthy gut, individuals should focus on a diet rich in fiber, fermented foods, and prebiotics¹⁰. Seeking advice from a healthcare professional or registered dietitian can offer tailored guidance for maintaining gut health¹¹. Thus, the impact of the human intake of food, drinks and medications should not be underestimated, as they might possess a profound effect on health in multidimensional aspects.

Diet and gut microbiota

The makeup of gut bacteria is heavily influenced by dietary choices. A diet packed with fiber, fruits and vegetables fosters the growth of beneficial gut bacteria. Conversely, a diet high in processed foods and sugar can lead to an overgrowth of harmful bacteria. Consuming specific dietary components like prebiotics and probiotics can significantly impact both the composition and function of gut microbiota¹². Beyond diet, factors such as stress, sleep, and physical activity also play a role in gut health¹³.

| Feature ^{5,6} | Allulose | Sugar alcohols | Other artificial sweeteners |
|------------------------|--|--|---|
| Source | Naturally occurring in small | Found naturally in some fruits and | Synthetic compounds |
| | quantities in some fruits and foods | vegetables; mostly manufactured | |
| Common | Allulose | Xylitol, erythritol, sorbitol, maltitol, | Aspartame, sucralose, saccharin, |
| Types | | mannitol, isomalt, lactitol | acesulfame potassium |
| Sweetness | About 70% as sweet as sugar | Generally, less sweet than sugar, varies by type | Hundreds to thousands of times sweeter than sugar |
| Calories | Less than 10% of the calories in sugar | Fewer calories than sugar, but more than allulose (e.g., erythritol: 0.2 cal/g) | Zero calories |
| Blood Sugar Impact | Does not substantially alter blood glucose or insulin levels | Minimal impact on blood sugar levels | No impact on blood sugar levels |
| Taste | Similar to sugar, no bitter aftertaste | Often have a cooling effect, can cause digestive issues in large amounts | Can have a bitter or metallic aftertaste |
| Safety | Recognized as safe by FDA and other authorities | Generally recognized as safe, but excessive consumption can cause digestive issues | Approved by FDA, but some studies suggest potential long- term health effects |

| Table 1: Comparison allulose, sugar alcohols and other artificial sweeteners | | Table 1: C | Comparison | allulose, | sugar | alcohols | and of | ther a | artificial | sweeteners | |
|--|--|------------|------------|-----------|-------|----------|--------|--------|------------|------------|--|
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Allulose and sugar alcohols: Low-calorie sweeteners with potential health benefits

Allulose and sugar alcohols have emerged as popular low-calorie sweeteners due to their minimal impact on blood sugar levels and their potential to improve metabolic health. Allulose, a rare sugar, is not readily absorbed by the body and has a negligible effect on blood glucose levels. Sugar alcohols, such as erythritol, xylitol, maltitol, and sorbitol, are partially digested and absorbed, resulting in a lower caloric content compared to traditional sugars. These sweeteners can be used as alternatives to sugar in various food products to help individuals reduce their overall calorie intake and improve their gut health¹⁴⁻¹⁸. Incorporating allulose and sugar alcohols into a balanced diet may contribute to better weight management and metabolic function.

Allulose and sugar alcohols: What are they?

Allulose is a low-calorie sweetener that is not fully absorbed by the body. Sugar alcohols, on the other hand, are partially digested and absorbed, providing fewer calories than regular sugar. Both can be used as substitutes for sugar in foods to aid in weight management and promote better gut health¹⁹⁻²². The key is to consume them in moderate amount to mitigate any risks associated with them, especially on the long-term use.

Allulose

Allulose is a rare monosaccharide that occurs naturally in small amounts in certain foods¹⁹. It has a similar structure to fructose but with a different arrangement of atoms and is not metabolized in the same way²⁰. Allulose is poorly absorbed by the body and has a minimal impact on blood glucose levels²¹.

Sugar alcohols

Sugar alcohols are a group of polyols that are derived from sugars but have different metabolic properties²². They are generally less sweet than sugar and have a lower caloric content²³. Common sugar alcohols include:

- **Erythritol**: A natural sugar alcohol found in fruits and fermented foods. It is approximately 60-70% as sweet as sugar and often has a cooling sensation²⁴.
- **Xylitol**: A natural sugar alcohol found in berries, mushrooms, and birch bark. It is about 100% as sweet as sugar and has a similar taste²⁵.

- **Maltitol**: A synthetic sugar alcohol derived from maltose. It is 70-90% as sweet as sugar and has a slightly different taste profile²⁶.
- **Sorbitol**: A natural sugar alcohol found in fruits and berries. It is 50-60% as sweet as sugar and has a slightly bitter aftertaste²⁷.

Chemical structure, effect and taste

Allulose, a scarce monosaccharide naturally present in limited quantities within certain fruits and vegetables, bears a structural similarity to fructose²⁸. Nevertheless, it is less sweet and has a negligible effect on insulin levels²⁹. Sugar alcohols, a group of compounds structurally related to sugars, possess unique metabolic characteristics^{27,30,31}. Generally, less sweet and lower in calories than sugar, common sugar alcohols include erythritol, xylitol, maltitol and sorbitol³². These sugar alcohols are often employed as sugar substitutes in food products marketed to individuals with diabetes or those seeking to reduce their sugar intake³³. Despite their lower caloric content, consuming excessive amounts of sugar alcohols may result in adverse consequences³⁴.

Caloric content, impact on blood sugar and applications in the food industry

Allulose is a low-calorie sugar substitute, containing only 0.4 calories per gram compared to 4 calories per gram in regular sugar. Research suggests that allulose may help regulate blood sugar levels by mitigating post-meal glucose spikes. Sugar alcohols, such as erythritol and sorbitol, also offer lower calorie content than sugar, ranging from 0.2-0.3 calories to 2.6 calories per gram, respectively. However, their impact on blood sugar can vary based on the specific compound and individual factors. Allulose and sugar alcohols have become popular in the food industry as tools to reduce sugar content and calories in various products. They can be used as sweeteners in a diverse range of applications, including baked goods, candies, beverages and dairy products. Nevertheless, the unique properties of each compound may influence their suitability for different applications³⁵⁻⁴¹.

Gut microbiota modulation

Sugar alcohols such as erythritol and xylitol have little to no effect on blood glucose levels, making them suitable for individuals with diabetes or those adhering to a low-carbohydrate eating plan⁴². Additionally, some

sugar alcohols like sorbitol can have a laxative effect if consumed in large amounts, so it's important for consumers to be mindful of their intake⁴³. Gut microbiota modulation involves using specific foods or compounds to influence the makeup and behavior of the bacterial community in the digestive tract⁴⁴. This can significantly impact various aspects of health, such as digestive processes, immune system function and mental well-being⁴⁵. Table 2 shows some important aspects of these types of sweetening agents^{35,36}, ^{39-43,46}. Emerging research suggests that allulose and sugar alcohols may have prebiotic effects, stimulating the growth of beneficial bacteria in the gut⁴⁷. Allulose has

been shown to increase the abundance of Bifidobacterium and Akkermansia muciniphila, which are associated with improved metabolic health⁴⁸. Sugar alcohols, particularly xylitol, have also been linked to increased levels of beneficial bacteria, as *Bifidobacterium* and *Lactobacillus*⁴⁹. These such changes in gut microbiota composition may have potential benefits for overall gut health and metabolic function⁵⁰. However, it is important to note that individual responses to allulose and sugar alcohols can vary, so moderation is key when consuming these ingredients⁵¹.

Table 2: Caloric content, impact on blood sugar, gastrointestinal effects and applications in the food industry.

| Compound | Caloric content | Impact on | Potential gastrointestinal effects | Common Applications |
|------------|-----------------|-------------|---|--|
| | (calories/gram) | blood sugar | | |
| Allulose | 0.4 | Minimal | Bloating, diarrhea (in high doses) | Baked goods, candies, beverages, ice cream |
| Erythritol | 0.2-0.3 | Minimal | Bloating, gas, diarrhea (in high doses) | Candies, chewing gum, baked goods |
| Xylitol | 2.4 | Minimal | Bloating, gas, diarrhea (in high doses) | Chewing gum, toothpaste, baked goods |
| Maltitol | 2.1 | Moderate | Bloating, gas, diarrhea (in high doses) | Candies, chocolate, baked goods |
| Sorbitol | 2.6 | Moderate | Bloating, gas, diarrhea (in high doses) | Candies, gum, diabetic-friendly foods |
| | | | | |

Mechanisms by which these substances modulate gut microbiota

The exact mechanisms by which allulose and sugar alcohols influence gut microbiota composition remain unclear. More research is necessary to fully comprehend how these substances interact with gut bacteria and their potential long-term health implications. Individuals should consult with healthcare professionals before making significant dietary changes involving these ingredients⁵²⁻⁵⁴. Several potential mechanisms have been suggested:

- **Prebiotic Effects:** Allulose and sugar alcohols may act as substrates for beneficial bacteria, stimulating their growth and metabolic activity⁵². The intricate relationship between alcohols and gut microbiota necessitates further investigation.
- Short-Chain Fatty Acid (SCFA) production: Gut bacteria can ferment sugar alcohols, resulting in the production of SCFAs, which offer numerous health benefits, such as improved insulin sensitivity and reduced inflammation⁵³. SCFAs also contribute to maintaining gut barrier integrity and supporting overall digestive health⁵⁴.
- Gut pH modulation: The fermentation of sugar alcohols can lower gut pH, creating an environment conducive to the growth of beneficial bacteria⁵⁵. This can help establish a healthy balance of gut microbiota and prevent the overgrowth of harmful bacteria⁵⁶. Additionally, a slightly acidic gut pH can enhance nutrient absorption and support overall digestive function⁵⁷.

Importance of a diverse and balanced gut microbiota for overall health

A varied and well-balanced gut microbiome is crucial for optimal health. A diverse microbiome can improve nutrient uptake, bolster the immune system and offer protection against various diseases⁵⁸. Dysbiosis, an imbalance in the gut microbiome, has been associated with a range of health issues, including obesity, type 2 diabetes, inflammatory bowel disease and mental health conditions⁵⁹. Thus, fostering a diverse and balanced gut microbiome through a nutritious diet rich in fiber, fermented foods and probiotics is essential for overall well-being⁶⁰. It's also important to avoid factors that can disrupt the microbiome, such as antibiotics, processed foods and chronic stress⁶¹. Maintaining a healthy gut microbiome can also enhance digestion and reduce inflammation throughout the body⁶². Adding prebiotic-rich foods like garlic, onions and bananas can further support the growth of beneficial bacteria in the gut⁶³.

Metabolic health benefits

Metabolic health benefits include improved digestion, reduced inflammation and better regulation of blood sugar levels⁶⁴. Additionally, a diverse gut microbiota has been associated with a lower risk of metabolic disorders such as obesity and diabetes⁶⁵. Maintaining a healthy gut microbiota through a balanced diet rich in fiber and fermented foods is crucial for promoting overall metabolic health¹². Furthermore, studies have shown that a healthy gut microbiota can also help in the absorption of nutrients and the production of certain vitamins essential for metabolic processes⁶⁶. Therefore, prioritizing gut health through dietary choices can have long-term benefits for overall metabolic function and well-being⁴⁵.

Impact on blood glucose levels: Allulose and sugar alcohols have been shown to have minimal impact on blood glucose levels. This is particularly beneficial for individuals with diabetes or prediabetes, as it can help to maintain stable blood sugar levels and reduce the risk of complications⁶⁷.

Potential role in weight management and obesity prevention: Allulose and sugar alcohols can contribute to weight management by reducing calorie intake. They can also help to increase satiety, leading to reduced food intake⁶⁸. Additionally, the prebiotic effects of these sweeteners may indirectly contribute to weight management by improving gut health and reducing inflammation⁶⁹. Effects on insulin sensitivity and metabolic syndrome risk factors: Allulose and sugar alcohols have been shown to improve insulin sensitivity and reduce the risk of metabolic syndrome¹. These effects may be mediated through various mechanisms, including the modulation of gut microbiota, reduced inflammation, and improved lipid metabolism¹⁹.

Potential challenges and considerations

While allulose and sugar alcohols offer potential health benefits, it is important to consider potential challenges and limitations. Excessive consumption of sugar alcohols can lead to gastrointestinal side effects, such as bloating, gas, and diarrhea⁷⁰. Additionally, individual tolerance to sugar alcohols may vary. Furthermore, the long-term effects of consuming allulose and sugar alcohols on gut microbiota composition and metabolic health are not fully understood⁷¹. More research is needed to determine the optimal dosage and duration of use for these sweeteners⁴⁸. Digestive issues associated with excessive consumption of sugar alcohols may be a concern for some individuals, especially those with sensitive stomachs⁷². It is recommended for each consumer to monitor their body's response and adjust consumption accordingly to avoid discomfort⁷³. Individual variability in tolerance to allulose and sugar alcohols should also be taken into consideration, as some people may experience bloating, gas or diarrhea with even small amounts⁷⁴. Consulting with a healthcare provider or nutritionist before incorporating these sweeteners into one's diet is advisable to ensure they are suitable for individual needs and health goals⁷⁵. The need for further research on long-term effects on gut microbiota and metabolic health is also crucial in order to fully understand the impact of these sweeteners on overall health⁷⁶. Additionally, staying informed about new studies and findings in this area can help individuals make more informed decisions about their dietary choices

Future research directions

While interest in allulose and sugar alcohols is growing, their long-term health effects and potential benefits remain incompletely understood¹². To gain a more comprehensive understanding of their impact on overall health, future research should focus on various populations, including children, pregnant women and individuals with specific health conditions³⁴. Additionally, exploring the interactions of these sweeteners with other dietary components and their role in metabolic health and well-being is crucial⁷⁷. Future studies should prioritize the following areas:

Long-term safety and efficacy: Long-term studies are needed to assess the safety and efficacy of allulose and sugar alcohols in human populations^{7,8}. Research should also explore their potential effects on gut health, metabolic function and weight management^{9,10}. A comprehensive understanding of their impact is essential for evidence-based recommendations regarding their consumption¹¹.

Impact on gut microbiota: The potential effects of these compounds on gut microbiota, a key factor in overall health, should be investigated^{12,13}. Studying the

interaction between allulose and sugar alcohols with gut bacteria can provide valuable insights into their impact on digestion and nutrient absorption¹⁴. This research can help determine if these sweeteners have any long-term effects on gut microbiota composition and function¹⁵.

Interactions with other nutrients: The interactions between allulose and sugar alcohols with other nutrients and dietary components should be examined^{16,17}. Understanding how these sweeteners may affect the absorption and utilization of essential vitamins and minerals in the body is important for assessing their overall impact on health¹⁸. Additionally, investigating potential synergistic or antagonistic effects with other dietary components can provide a more comprehensive understanding of their physiological effects¹⁹.

Consumer acceptance and preferences: Studies on consumer acceptance and preferences for allulose and sugar alcohols can inform product development and marketing strategies^{20,21}. Furthermore, exploring the potential long-term health implications of regular consumption of these sweeteners can help guide recommendations for their use in various populations²². It is also important to consider the environmental impact of producing and using these sweeteners as alternatives to traditional sugars²³.

CONCLUSIONS

Allulose and sugar alcohols are low-calorie sweeteners with potential health benefits. These sweeteners can positively impact gut microbiota, leading to a healthier gut environment and reduced risk of metabolic disorders. However, moderation is key and individual tolerance varies. Future research should delve into the mechanisms behind these sweeteners' effects and their long-term impact on human health. By understanding the complex interactions between these sweeteners, gut microbiota and metabolic health, it is possible to create evidence-based dietary guidelines for optimal health. Incorporating gut health into metabolic health and disease prevention strategies is essential for personalized nutrition. By exploring the relationship between gut microbiota and metabolic health, development of targeted interventions to promote wellbeing and reduce chronic disease risk could be attained.

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AUTHOR'S CONTRIBUTIONS

Eissa ME: conceived the idea, writing the manuscript, literature survey, formal analysis, critical review.

CONFLICT OF INTEREST

None to declare.

REFERENCES

- Bae HR, Shin SK, Han Y, Yoo JH, Kim S, Young HA, Kwon EY. D-allulose ameliorates dysregulated macrophage function and mitochondrial NADH homeostasis, mitigating obesity-induced insulin resistance. Nutrients. 2023 Sep 29;15(19):4218. https://doi.org/10.3390/nu15194218
- Magnuson BA, Carakostas MC, Moore NH, Poulos SP, Renwick AG. Biological fate of low-calorie sweeteners. Nutr Rev 2016; 74(11):670-689. https://doi.org/10.1093/nutrit/nuw032
- Livesey G. Health potential of polyols as sugar replacers, with emphasis on low glycaemic properties. Nutr Res Rev 2003;16(2):163-191. https://doi.org/10.1079/NRR200371
- Lobach AR, Roberts A, Rowland IR. Assessing the in vivo data on low/no-calorie sweeteners and the gut microbiota. Food Chem Toxicol 2019; 124:385-399. https://doi.org/10.1016/j.fct.2018.12.005
- Mya Care. Allulose vs. Other sweeteners: How does it compare? https://myacare.com/blog/allulose-vs-othersweeteners-how-does-it-compare
- 6. Mayo Clinic. Artificial sweeteners and other sugar substitutes.
- Villanueva-Millán MJ, Pérez-Matute P, Oteo JA. Gut microbiota: A key player in health and disease. J Physiol Biochem 2015; 71(3):509-525. https://doi.org/10.1007/s13105-015-0390-3
- Hills RD Jr, Pontefract BA, Mishcon HR, et al. Gut microbiome: Profound implications for diet and disease. nutrients. 2019;11(7):1613. https://doi.org/10.3390/nu11071613
- Kim YT, Mills DA. Exploring the gut microbiome: probiotics, prebiotics, synbiotics, and more. Food Sci Biotechnol 2024;33(3):123-134. https://doi.org/10.1007/s10068-024-01620-1
- Marchesi JR, Adams DH, Fava F, Hermes GD, Hirschfield GM, Hold G, et al. The gut microbiota and host health: a new clinical frontier. Gut 2016; 65(2):330-339. https://doi.org/10.1136/gutjnl-2015-309990
- 11. Rinninella E, Raoul P, Cintoni M, et al. What is the healthy gut microbiota composition? A changing ecosystem across age, environment, diet, and diseases. Microorganisms. 2019;7(1):14. https://doi.org/10.3390/microorganisms7010014
- Valdes AM, Walter J, Segal E, Spector TD. Role of the gut microbiota in nutrition and health. BMJ 2018; 361:k2179. http://doi:10.1136/bmj.k2179
- Zmora N, Suez J, Elinav E. You are what you eat: Diet, health and the gut microbiota. Nat Rev Gastroenterol Hepatol 2019;16(1):35-56. https://doi.org/10.1038/s41575-018-0061-2
- Clifford J, Maloney K. Sugar and sweeteners. Colorado State University Extension 2016 Jan.
- Health. Best and Worst Artificial Sweeteners, Ranked. 2023 Oct 3. https://www.health.com/best-and-worstartificial-sweeteners-7974926
- Understanding sugar alcohol: A complete guide for food producers and brands. Medallion Labs 2024 Apr 10. https://www.medallionlabs.com/blog/understanding-sugaralcohols/
- 17. Clean Plates Editorial Team. Sugar Substitutes: Types, Benefits, Dangers & Brands. Clean Plates 2020 Oct 3.
- Ajmera R. Can Allulose Help With Weight Loss? Plus benefits, downsides, and safety. Lose It!. 2023 Dec 5.
- Di Marino A, Hazen S. What is allulose? Cleveland Clinic Health Essentials 2022 Aug 26. https://health.clevelandclinic.org/what-is-allulose
- Benisek A. Allulose: What to Know. WebMD. 2023 Apr 14. https://www.webmd.com/diet/features/what-is-allulose
- 21. Healthline Editorial Team. Allulose: What It Is, Benefits, Risks, and More. Healthline 2023. https://www.healthline.com/nutrition/allulose

- 22. Loescher WH. Physiology and metabolism of sugar alcohols in higher plants. Physiologia Plantarum 1987 Jul 1;70(3).
 - https://doi.org/10.1111/j.1399-3054.1987.tb02857.x
- Hamano H. Functional properties of sugar alcohols as lowcalorie sugar substitutes. Food Indus Nut 1997; 2(1):1-6.
- 24. Godswill AC. Sugar alcohols: Chemistry, production, health concerns and nutritional importance of mannitol, sorbitol, xylitol, and erythritol. Int J Adv Acad Res Sci Technol Eng 2017; 3(2):31-45.
- Mäkinen KK. Sugar alcohols. Functional Foods: Designer Foods, Pharmafoods, Nutraceuticals 1994. Boston, MA: Springer US, 219-241..
- Mitsuhashi M, Hirao M, Sugimoto K, inventors; Hayashibara Co Ltd, assignee. Low calorie sweetener mixture of maltitol and maltotritol. United States patent US 3,705,039. 1972 Dec 5.
- Grembecka M. Sugar alcohols—their role in the modern world of sweeteners: A review. European Food Res Tech 2015 Jul; 241:1-4. https://doi.org/10.1007/s00217-015-2437-7
- 28. Van Laar AD, Grootaert C, Van Camp J. Rare mono-and disaccharides as healthy alternative for traditional sugars and sweeteners? Critical Reviews Food Sci Nutrition 2021 Mar 9; 61(5):713-41.

https://doi.org/10.1080/10408398.2020.1743966

- 29. Hossain A, Yamaguchi F, Matsuo T, et al. Rare sugar Dallulose: Potential role and therapeutic monitoring in maintaining obesity and type 2 diabetes mellitus. Pharmacology & therapeutics. 2015 Nov 1; 155:49-59. https://doi.org/10.1016/j.pharmthera.2015.08.004
- Evrendilek GA. Sugar alcohols (polyols). Sweeteners: nutritional aspects, applications, and production technology 2012 May 14;14(2):56-60.
- Ibrahim OO. Sugars alcohols: Chemical structures, manufacturing, properties and applications. EC Nutrition. 2016; 4(2):817-24.
- 32. Msomi NZ, Erukainure OL, Islam MS. Suitability of sugar alcohols as antidiabetic supplements: A review. J Food Drug Anal 2021;29(1):1. https://doi.org/10.38212/2224-6614.3107
- 33. Singh P, Ban YG, Kashyap L, Siraree A, Singh J. Sugar and sugar substitutes: recent developments and future prospects. Sugar and sugar derivatives: changing consumer preferences. 2020:39-75. https://doi.org/10.1007/978-981-15-6663-9_4
- 34. Awuchi CG, Echeta KC. Current developments in sugar alcohols: Chemistry, nutrition, and health concerns of sorbitol, xylitol, glycerol, arabitol, inositol, maltitol, and lactitol. Int J Adv Acad Res 2019;5(11):1-33.
- 35. What is Allulose? A Guide to Allulose as a Sugar-Substitute. Hometown Hero. 2024 Oct 9. Available from: https://hometownhero.com/learn/allulose-a-sugaralternative-thats-actually-healthier-than-sugar/
- 36. Tani Y, Tokuda M, Nishimoto N, Yokoi H, Izumori K. Allulose for the attenuation of postprandial blood glucose levels in healthy humans: A systematic review and metaanalysis. PLoS ONE 2023 Apr 6;18(4):e0281150. https://doi.org/10.1371/journal.pone.0281150
- What You Should Know About Sugar Alcohols. Cleveland Clinic 2024 Jun 17.
- How healthy is sugar alcohol? Harvard Health 2023 Dec 18.
- Why Allulose Could be the Next Big Thing in Sweeteners. The Food Institute 2022 Jul 25.
- 40. Types of Sweeteners: Sugars, Substitutes & More. Webstaurant Store 2024 Oct 4.
- 41. Sugars That Are Metabolized Differently Than Traditional Sugars. FDA.
- 42. Glezer-Jones D. Xylitol, Erythritol, Stevia, Maltitol, and Isomalt and their Impact on Blood Sugar Levels. Caring Candies. 2024 Sep 5.
- Werrett A. Sorbitol Laxative Effect: Understanding the right dose. MedShun 2024 Jul 30.

- 44. Vernocchi P, Del Chierico F, Putignani L. Gut microbiota metabolism and interaction with food components. Int J Mol Sci 2020 May 23;21(10):3688. https://doi.org/10.3390/ijms21103688
- 45. Linus Pauling Institute. Gut Health In Brief. Oregon State University.
- 46. Chattopadhyay S, Raychaudhuri U, Chakraborty R. Artificial sweeteners - A review. J Food Sci Technol 2014; 51(4):611-621. https://doi.org/10.1007/s13197-011-0571-1
- 47. Payne AN, Chassard C, Lacroix C. Gut microbial adaptation to dietary consumption of fructose, artificial sweeteners and sugar alcohols: implications for hostmicrobe interactions contributing to obesity. Obesity Rev 2012 Sep;13(9):799-809.
- https://doi.org/10.1111/j.1467-789X.2012.01009.x 48. Daniel H, Hauner H, Hornef M, Clavel T. Allulose in human diet: the knowns and the unknowns. Br J Nutr 2021;128(2):172-178.
- https://doi.org/10.1017/S0007114521003172
- 49. Salli K, Lehtinen MJ, Tiihonen K, Ouwehand AC. Xylitol's health benefits beyond dental health: A comprehensive review. Nutrients 2019 Aug 6;11(8):1813. https://doi.org/10.3390/nu11081813
- 50. Are Sugar Alcohols Safe? The Truth About Xylitol and LifeSpa. Ervthritol Risks. 2024 Aug 14 https://lifespa.com/health-topics/weight-management/aresugar-alcohols-safe/
- 51. Wee M, Tan V, Forde C. A comparison of psychophysical dose-response behaviour across 16 sweeteners. Nutrients 2018 Nov 2;10(11):1632. https://doi.org/10.3390/nu10111632
- 52. Aljeradat B, Kumar D, Abdulmuizz S, et al. Neuromodulation and the gut-brain axis: Therapeutic mechanisms and implications for gastrointestinal and neurological disorders. Pathophysiol 2024 May 17; 31(2):244-68.

https://doi.org/10.3390/pathophysiology31020019

- 53. Van Hul M, Cani PD, Petitfils C, et al. What defines a healthy gut microbiome? Gut 2024 Nov 1; 73(11):1893-908. https://doi.org/10.1136/gutjnl-2024-333378
- 54. Ma J, Piao X, Mahfuz S, Long S, Wang J. The interaction among gut microbes, the intestinal barrier and short chain fatty acids. Animal Nutri 2022 Jun 1; 9:159-74. https://doi.org/10.1016/j.aninu.2021.09.012
- 55. How Does Your Gut Microbiome Impact Your Overall Health? Healthline. 2024.
- 56. Paul P, Kaul R, Chaari A. Renal health improvement in diabetes through microbiome modulation of the gutkidney axis with biotics: a systematic and narrative review of randomized controlled trials. Int J Mol Sci 2022 Nov 27; 23(23):14838. https://doi.org/10.3390/ijms232314838
- 57. Zambelli RA, de Mendonça LG. Application of probiotics in food industry: A promising scope for improving food quality. CRC Press. Probiotics: 282-304.
- 58. Bengmark S. Gut microbiota, immune development and function. Pharmacological Res 2013 Mar 1; 69(1):87-113. https://doi.org/10.1016/j.phrs.2012.09.002
- 59. Eissa M. Investigating the gut microbiome's role in antibiotic resistance in companion animals. J Res Vet Sci 2024 May 20; 2(4):159-174. https://doi.org/10.5455/JRVS.20240429060752
- 60. Eissa M. The gut microbiome: A potential therapeutic path in complementary medicine. J Res Complement Med 2024;10(1):45-58. https://doi.org/10.5455/jrcm.20240509063048
- 61. Eissa ME. Microbial metagenomics and the personalized treatment of periodontal disease. Eur J Dent Res 2024;1(1):1-16

https://doi.org/10.5455/EJDR.20240527092603

62. Plat C. The gut microbiota: Key players in nutrient metabolism and health. Insights Nutr Metab 2024; 8(2):45-52.

63. Sadeghpour Heravi F. Gut Microbiota and Autoimmune Diseases: Mechanisms, Treatment, Challenges, and Future Recommendations. Curr Clin Microbiol Rep 2024 Mar;11(1):18-33.

https://doi.org/10.1007/s40588-023-00213-6

- 64. Barber TM, Kabisch S, Pfeiffer AFH, Weickert MO. The Health Benefits of Dietary Fibre. Nutrients 2020;12(10):3209. https://doi.org/10.3390/nu12103209
- 65. Sasidharan Pillai S, Gagnon CA, Foster C, Ashraf AP. Exploring the gut microbiota: Key insights into its role in obesity, metabolic syndrome, and type 2 diabetes. J Clin Endocrinol Metab 2024;109(11):2709-2719. https://doi.org/10.1210/clinem/dgae499
- 66. Wang L, Wang S, Zhang Q, He C, Fu C, Wei Q. The role of the gut microbiota in health and cardiovascular diseases. Mol Biomed 2022;3:30. https://doi.org/10.1186/s43556-022-00091-2
- 67. Cayabyab KB, Shin MJ, Heimuli MS, et al. The metabolic and endocrine effects of a 12-week allulose-rich diet. Nutrients 2024 Jan; 16(12):1821. https://doi.org/10.3390/nu16121821
- 68. Franchi F, Yaranov DM, Rollini F, et al. Effects of dallulose on glucose tolerance and insulin response to a standard oral sucrose load: results of a prospective, randomized, crossover study. BMJ Open Diabetes Res Care. 2021; 9: e001939. https://doi.org/10.1136/bmjdrc-2020-001939
- 69. Verma MK, Tripathi M, Singh BK. Dietary determinants of metabolic syndrome: Focus on the obesity and Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD). https://doi.org/10.5772/intechopen.114832
- 70. Singh SA, Singh S, Begum RF, Vijayan S, Vellapandian C. Unveiling the profound influence of sucralose on metabolism and its role in shaping obesity trends. Frontiers in Nutrition. 2024 Jul 2;11:1387646. https://doi.org/10.3389/fnut.2024.1387646
- 71. Klein S, Sheard NF, Pi-Sunyer X, et al. Weight management through lifestyle modification for the prevention and management of type 2 diabetes: Rationale and strategies: A statement of the American Diabetes Association, the North American Association for the Study of Obesity, and the American Society for Clinical Nutrition. Diabetes Care 2004 Aug 1;27(8):2067-73. https://doi.org/10.2337/diacare.27.8.2067
- 72. Arnone D, Chabot C, Heba AC, et al. Sugars and gastrointestinal health. Clinical Gastroenterology and Hepatology. 2022 Sep 1;20(9):1912-24. https://doi.org/10.1016/j.cgh.2021.12.011
- 73. Yuma T, Tokuda M, Nishimoto N, Yokoi H, Izumori K. Allulose for the attenuation of postprandial blood glucose levels in healthy humans: A systematic review and metaanalysis. PLoS One 2023 Apr 6;18(4):e0281150. https://doi.org/10.1371/journal.pone.0281150
- 74. Coultate T. Food: The chemistry of its components. Royal Soc Chem 2023; Oct 11.
- 75. All. Discover Real Food in Texas. Discover Real Food in Texas. 2024 [cited 2024 Nov 4].
- 76. Ruiz-Ojeda FJ, Plaza-Díaz J, Sáez-Lara MJ, Gil A. Effects of sweeteners on the gut microbiota: A review of experimental studies and clinical trials. Adv Nutri 2019 Jan 1; 10:S31-48. https://doi.org/10.1093/advances/nmy037
- 77. Gopalakrishnan NK, Balasubramanian B, Kundapur R, et al. Unraveling connections with artificial sweeteners and their impact on human health: A comprehensive review. Food 2024 Oct; 5(5):e184. https://doi.org/10.1002/efd2.184